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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/864,675	05/23/2001	Mark Marchionni	04585/049002	3830

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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/864,675	MARCHIONNI, MARK
Examiner	**Art Unit**
Christopher Nichols, Ph.D.	1647

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-69* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims **1-9, and 48-52 (each in part)**, drawn to a *method for increasing the mitogenesis, survival, growth, or differentiation of a cell* comprising administering a NRG-2 polypeptide, classified in class 514, subclass 2, for example.

II. Claims **10 and 50-52 (each in part)**, drawn to a *method for inducing myelination of a neuronal cell by a glial cell* comprising contacting said glial cell with a NRG-2 polypeptide, classified in class 514, subclass 2, for example.

III. Claims **11-19 and 50-52 (each in part)**, drawn to a *method of increasing the cardiomyocyte survival, cardiomyocyte proliferation, cardiomyocyte growth, or cardiomyocyte differentiation in a mammal* in need thereof, said method comprising administering a NRG-2 polypeptide to said mammal, classified in class 514, subclass 2, for example.

IV. Claims **20-25 and 50-52 (each in part)**, drawn to a *method of affecting cellular communication* between a neuronal-associated cell and a neuronal cell in a mammal comprising administering a NRG-2 polypeptide to said mammal, classified in class 514, subclass 2, for example.

V. Claims **20-26, 42, and 50-52 (each in part)**, drawn to a *method of affecting cellular communication* between a neuronal-associated cell and a neuronal cell in a mammal comprising administering a NRG-2 polypeptide to said mammal

wherein said administering comprises administering a purified NRG-2 polypeptide-producing cell, classified in class 514, subclass 2, for example.

VI. Claims **27-40 and 50-52 (each in part)**, drawn to a *method for the treatment or prophylaxis of a pathophysiological condition of the nervous system* in a mammal comprising administering a therapeutically effective amount of a recombinant NRG-2 polypeptide to said mammal, classified in class 514, subclass 2, for example.

VII. Claims **27-42 and 50-52 (each in part)**, drawn to a *method for the treatment or prophylaxis of a pathophysiological condition of the nervous system* in a mammal comprising administering a therapeutically effective amount of a recombinant NRG-2 polypeptide to said mammal wherein said administering comprises administering a purified NRG-2 polypeptide-producing cell, classified in class 514, subclass 2, for example.

VIII. Claims **43-45 and 50-52 (each in part)**, drawn to a *method for the treatment of a tumor* comprising inhibiting proliferation of a tumor cell said inhibiting comprising administering to a subject in need thereof an effective amount of an antibody, classified in class 424, subclass 130.1, for example.

IX. Claims **46 and 50-52 (each in part)**, drawn to a *method for treatment of neurofibromatosis* comprising inhibiting proliferation of a tumor cell said inhibiting comprising administering to a subject in need thereof an effective amount of an antibody, classified in class 424, subclass 130.1, for example.

X. Claims **47, 49, and 50-52 (each in part)**, drawn to a *method for inhibiting proliferation* of a cell comprising contacting said cell with an effective amount of an antibody, classified in class 424, subclass 130.1, for example.

XI. Claims **53 and 54**, drawn to a substantially pure *NRG-2 polypeptide*, classified in class 530, subclass 300, for example.

XII. Claims **55-57 and 59 (each in part)**, drawn to a substantially pure *nucleic acid* comprising SEQ ID NO: 2 or 4 and vectors comprising same, classified in class 536, subclass 23.1, for example.

XIII. Claims **55, 56, 57, 60, and 61 (each in part)**, drawn to a substantially pure *nucleic acid* comprising SEQ ID NO: 2 or 4 and gene therapy vectors and cells comprising same, classified in class 514, subclass 44, for example.

XIV. Claim **58**, drawn to an *antisense* molecule, classified in class 536, subclass 24.5, for example.

XV. Claims **62-64**, drawn to a *non-human transgenic animal*, classified in class 800, subclass 8, for example.

XVI. Claim **65 and 69**, drawn to an *antibody* and kit comprising same, classified in class 530, subclass 387.1, for example.

XVII. Claim **66**, drawn to a *method of detecting the presence of a NRG-2 polypeptide* in a sample comprising contacting said sample with the antibody of claim 65, classified in class 435, subclass 7.1, for example.

XVIII. Claims **67 and 68**, drawn to a *method of diagnosing an increased likelihood of developing a NRG-2-related disease* or condition in a test subject comprising analyzing nucleic acid molecules, classified in class 435, subclass 6, for example.

2. The inventions are distinct, each from the other because of the following reasons:

3. Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive Inventions that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: Inventions I, II, III, IV, V, VI, VII, VIII, IX, X, XVII and XVIII are directed to methods that are distinct both physically and functionally, and are not required one for the other. Invention I requires search and consideration of increasing the mitogenesis, survival, growth, or differentiation of a cell, which is not required by any of the other Inventions. Invention II requires search and consideration of inducing myelination, which is not required by any of the other Inventions. Invention III requires search and consideration of cadiomyocytes, which is not required by any of the other Inventions. Invention IV requires search and consideration of affecting cellular communication, which is not required by any of the other Inventions. Invention V requires search and consideration of affecting cellular communication via administering a cell as a therapeutic agent, which is not required by any of the other Inventions. Invention VI requires search and consideration of a method for treatment or prophylaxis of a pathophysiological condition of the nervous system, which is not required by any of the other Inventions. Invention VII requires search and consideration of a method for treatment or prophylaxis of a pathophysiological condition of the nervous system via

administering a cell as a therapeutic agent, which is not required by any of the other Inventions. Invention VIII requires search and consideration of a method for treatment of a tumor, which is not required by any of the other Inventions. Invention IX requires search and consideration of a method for treatment of neurofibromatosis, which is not required by any of the other Inventions. Invention X requires search and consideration of inhibiting proliferation, which is not required by any of the other Inventions. Invention XVII requires search and consideration of determining the presence or amount of a polypeptide in a sample, which is not required by any of the other Inventions. Invention XVIII requires search and consideration of determining the presence or amount of a nucleic acid molecule in a sample, which is not required by any of the other Inventions.

4. Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive groups that are directed to different products, restriction is deemed to be proper because these products constitute patentably distinct inventions for the following reasons. Inventions XI, XII, XIII, XIV, XV, XVI, and XVII are directed to products that are distinct both physically and functionally, are not required one for the other, and are therefore patentably distinct. While the polypeptide of Invention XI can be prepared by processes which are materially different from nucleic acid of Invention XII, the nucleic acid of Invention XIII, purification from the non-human transgenic animal of Invention XV, or purified using the antibody of Invention XVI such as by chemical synthesis. Additionally, the nucleic acid of Invention XII can be used in materially different methods other than to make the polypeptide of Invention XI, the antisense molecule of Invention XIV, the non-human transgenic animal of Invention XV, it can be used in materially different methods, such as a probe in nucleic acid

hybridization assays. The antibody of Invention XVI is not required to make or use the nucleic acid of Invention XII. Additionally, the nucleic acid of Invention XIII can be used in materially different methods other than to make the polypeptide of Invention XI, the antisense molecule of Invention XIV, the non-human transgenic animal of Invention XV, such as a probe in nucleic acid hybridization assays. The antibody of Invention XVI is not required to make or use the nucleic acid of Invention XIII. The antisense molecule can be made through materially different methods than the nucleic acids of Invention XII and XIII such a chemical synthesis. The polypeptide of Invention XI, the non-human transgenic animal of Invention XV, and the antibody of Invention XVI are not required to make or use the antisense molecule of Invention XIV. The non-human transgenic animal of Invention XV does not require the polypeptide of Invention XI, the antisense molecule of Invention XIV, or the antibody of Invention XVI to be made or used. While the nucleic acids of Inventions XII and XIII can be used to make the non-human transgenic animal of Invention XV it can be made through materially different methods such as animal husbandry or embryo mutagenesis. Finally, although the antibody of Invention XVI can be used to obtain the polypeptide of Invention XI it can also be used in materially different methods, such as in various diagnostic (e.g., as a probe in immunoassays or immunochromatography), or therapeutic methods. The nucleic acids of Inventions XII and XIII, the antisense molecule of Invention XIV, the non-human transgenic animal of Invention XV are not required to make or use the antibody of Invention XVI.

5. Inventions XI and each of I, II, III, IV, V, VI, and VII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another

materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide of Invention XI can be used to make antibodies.

6. Inventions XII and XVIII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acids of XII can be used in gene therapy.

7. Inventions XIII and each of V, VII, and XVIII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the gene therapy vectors of Invention XIII can be used to recombinantly express polypeptides.

8. Inventions XVI and each of VIII, IX, X, and XVII are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Invention XVI can be used to purify polypeptides from natural sources.

9. Inventions XI and each of VIII, IX, X, XVII, and XVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have

different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of Inventions XI and each of VIII, IX, X, XVII, and XVIII are unrelated product and methods, wherein each is not required, one for another. For example, the claimed methods of Inventions VIII, IX, X, XVII, and XVIII do not recite the use or production of the polypeptide of Invention XI.

10. Inventions XII and each of I, II, III, IV, V, VI, VII, VIII, IX, X, and XVII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of Inventions XIII and each of I, II, III, IV, V, VI, VII, VIII, IX, X, and XVII are unrelated product and methods, wherein each is not required, one for another. For example, the claimed methods of Inventions I, II, III, IV, V, VI, VII, VIII, IX, X, and XVII do not recite the use or production of the nucleic acid of Invention XII.

11. Inventions XIII and each of I, II, III, IV, VI, VIII, IX, X, XVII, and XVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of Inventions XIII and each of I, II, III, IV, VI, VIII, IX, X, XVII, and XVIII are unrelated product and methods, wherein each is not required, one for another. For example, the claimed methods of Inventions I, II, III, IV, VI, VIII, IX, X, XVII, and XVIII do not recite the use or production of the gene therapy constructs of Invention XIII.

12. Inventions XIV and each of I, II, III, IV, V, VI, VII, VIII, IX, X, XVII, and XVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of Inventions XIV and each of I, II, III, IV, V, VI, VII, VIII, IX, X, XVII, and XVIII are unrelated product and methods, wherein each is not required, one for another. For example, the claimed methods of Inventions I, II, III, IV, V, VI, VII, VIII, IX, X, XVII, and XVIII do not recite the use or production of the antisense molecule of Invention XIV.

13. Inventions XV and each of I, II, III, IV, V, VI, VII, VIII, IX, X, XVII, and XVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of Inventions XV and each of I, II, III, IV, V, VI, VII, VIII, IX, X, XVII, and XVIII are unrelated product and methods, wherein each is not required, one for another. For example, the claimed methods of Inventions I, II, III, IV, V, VI, VII, VIII, IX, X, XVII, and XVIII do not recite the use or production of the non-human transgenic animal of Invention XV.

14. Inventions XVI and each of I, II, III, IV, V, VI, VII, and XVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions of Inventions XVI and each of I, II, III, IV, V, VI, VII, and XVIII are unrelated product and methods, wherein each is not required,

one for another. For example, the claimed methods of Inventions I, II, III, IV, V, VI, VII, and XVIII do not recite the use or production of the antibody of Invention XVI.

15. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

16. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, separate search requirements, and/or different classification, restriction for examination purposes as indicated is proper.

17. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

CJN
August 25, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER